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L19 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2002 ACS

AN 2002:519375 HCAPLUS

TI IL-27, a heterodimeric cytokine composed of EBI3 and p28 protein, induces proliferation of naive CD4+ T cells

AU Pflanz, Stefan; Timans, Jackie C.; Cheung, Jeanne; Rosales, Rency; Kanzler, Holger; Gilbert, Jonathan; Hibbert, Linda; Churakova, Tatyana; Travis, Marilyn; Vaisberg, Elena; Blumenschein, Wendy M.; Mattson, Jeanine D.; Wagner, Janet L.; To, Wayne; Zurawski, Sandra; McClanahan, Terrill K.; Gorman, Daniel M.; Bazan, J. Fernando; Malefyt, Rene De Waal; Rennick, Donna; Kastelein, Robert A.

CS DNAX Research Institute, Palo Alto, CA, 94304, USA

SO Immunity (2002), 16(6), 779-790

CODEN: IUNIEH; ISSN: 1074-7613

PB Cell Press

DT Journal

LA English

CC 15-5 (Immunochemistry)

Section cross-reference(s): 3

AB An efficient Th1-driven adaptive immune response requires activation of the T cell **receptor** and secretion of the T cell stimulatory cytokine IL-12 by activated antigen-presenting cells. IL-12 triggers Th1 polarization of naive CD4+ T cells and secretion of IFN- γ . The authors describe a new heterodimeric cytokine termed IL-27 that consists of EBI3, an IL-12p40-related protein, and p28, a newly discovered IL-12p35-related polypeptide. IL-27 is an early product of activated antigen-presenting cells and drives rapid clonal expansion of naive but not memory CD4+ T cells. It also strongly synergizes with IL-12 to trigger IFN- γ prodn. of naive CD4+ T cells. IL-27 mediates its biol. effects through the orphan cytokine **receptor** **WSX**-1/TCCR.

ST interleukin 27 EBI3 p28 protein subunit; proliferation T cell interleukin 27

IT INDEXING IN PROGRESS

IT Interleukins
 RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
 (27; is composed of EBI3 and p28 proteins and induces proliferation of naive CD4+ T-cells)

IT Proteins
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (EBI3 (Epstein-Barr-induced 3); as subunit of interleukin-27)

IT Cell proliferation
 (T cell; of naive CD4+ T-cells induced by interleukin-27)

IT Receptors
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (TCCR; interleukin-27 is ligand for)

IT Human
 Mouse
 (characterization of interleukin-27 of)

IT Dendritic cell
 Monocyte
 (co-expression of p28 and EBI3 proteins by)

IT Protein sequences
 (for interleukin-27 p28 of human and mouse)

IT Chromosome
 (human 16; interleukin-27 p28 subunit gene maps to)

IT Interleukin 12
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (interferon-.gamma. prodn. by interleukin-27-stimulated T-cells is enhanced by)

IT CD4-positive T cell
 (interleukin-27 is composed of EBI3 and p28 proteins and induces proliferation of naive CD4+ T-cells)

IT Lymphocyte
 (natural killer cell; interleukin-27 enhances interferon-.gamma. prodn. by)

IT Molecular association
 (of EBI3 and p28 proteins)

IT T cell (lymphocyte)
 (proliferation; of naive CD4+ T-cells induced by interleukin-27)

IT Interferons
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (.gamma.; prodn. by interleukin-27-stimulated T-cells is enhanced by interleukin-12)

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- (31) Yoshida, H; Immunity 2001, V15, P569 HCAPLUS

L19 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2002 ACS

AN 2002:519372 HCAPLUS

TI Further checkpoints in Th1 development

AU Robinson, Douglas S.; O'Garra, Anne

CS Allergy and Clinical Immunology and Leukocyte Biology Faculty of Medicine,
Imperial College, London, SW7 2AK, UK

SO Immunity (2002), 16(6), 755-758

CODEN: IUNIEH; ISSN: 1074-7613

PB Cell Press

DT Journal; General Review

LA English

CC 15-0 (Immunochemistry)

AB Tight control of Th1 immunity is essential to prevent immunopathol.
Central to control of the IFN- γ gene is the transcription factor
T-bet, whose induction is Stat-1 dependent. IL-12 is dominant in
directing Th1 development, while synergizing with IL-18 for IFN- γ
prod. from differentiated Th1 cells. In this issue of Immunity, IL-27 is
described, which acts in synergy with IL-12 early in Th1 development from
naive T cells via the **receptor** TCCR/WSX-1. We review
the coordination of these checkpoints in Th1 development and function.

ST review Th1 lymphocyte development cytokine

IT INDEXING IN PROGRESS

IT Hematopoiesis

(T-cell lymphopoiesis; checkpoints in Th1 development)

IT Cytokines

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(checkpoints in Th1 development)

IT T cell (lymphocyte)

(helper cell/inducer, TH1; checkpoints in Th1 development)

RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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L19 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2002 ACS

AN 2001:803366 HCAPLUS

DN 136:84560

TI **WSX-1** is required for the initiation of Th1 responses and
resistance to L. major infection

AU Yoshida, Hiroki; Hamano, Shinjiro; Senaldi, Giorgio; Covey, Todd;
Faggioni, Raffaella; Mu, Sharon; Xia, Min; Wakeham, Andrew C.; Nishina,
Hiroshi; Potter, Julia; Saris, Chris J. M.; Mak, Tak W.

CS The Amgen Institute Ontario Cancer Institute and Departments of Medical
Biophysics and Immunology, University of Toronto, Toronto, ON, M5G 2C1,
Can.

SO Immunity (2001), 15(4), 569-578

CODEN: IUNIEH; ISSN: 1074-7613

PB Cell Press

DT Journal

LA English

CC 15-8 (Immunochemistry)

AB **WSX-1** is a class I cytokine receptor with homol. to
the IL-12 receptors. The physiol. role of **WSX-1**,
which is expressed mainly in T cells, was investigated in gene-targeted
WSX-1-deficient mice. IFN- γ prodn. was reduced in isolated
WSX-1^{-/-} T cells subjected to primary stimulation in vitro to
induce Th1 differentiation but was normal in fully differentiated and
activated **WSX-1**^{-/-} Th1 cells that had received secondary
stimulation. **WSX-1**^{-/-} mice were remarkably susceptible to
Leishmania major infection, showing impaired IFN- γ prodn. early in
the infection. However, IFN- γ prodn. during the later phases of the
infection was not impaired in the knockout. **WSX-1**^{-/-} mice also
showed poorly differentiated granulomas with dispersed accumulations of
mononuclear cells when infected with bacillus Calmette-Guerin (BCG).
Thus, **WSX-1** is essential for the initial mounting of Th1
responses but dispensable for their maintenance.

ST receptor WSX1 Th1 cytokine Leishmania infection

IT Leishmania major

(**WSX-1** is required for the initiation of Th1 responses and
resistance to L. major infection)

IT Interleukin 4

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(**WSX-1** is required for the initiation of Th1 responses and
resistance to L. major infection)

IT Mycobacterium BCG

(**WSX-1** is required for the initiation of Th1 responses and
resistance to L. major infection and)

IT Cytokine receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(**WSX-1**; **WSX-1** is required for the initiation of Th1
responses and resistance to L. major infection)

IT T cell (lymphocyte)

(activation; **WSX-1** is required for the initiation of Th1
responses and resistance to L. major infection)

IT T cell (lymphocyte)
(helper cell/inducer, TH1; **WSX-1** is required for the
initiation of Th1 responses and resistance to L. major infection)

IT Interferons
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(.gamma.; **WSX-1** is required for the initiation of Th1
responses and resistance to L. major infection)

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L19 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2002 ACS

AN 1998:546453 HCAPLUS

DN 129:265447

TI Hemostatic and air leak sealing effects of rapidly curable glues from
gelatin, poly(L-glutamic acid), and carbodiimide

AU Tabata, Y.; Otani, Y.; Ikada, Y.

CS Res. Cent. Biomed. Eng., Kyoto Univ., Kyoto, 606-8507, Japan

SO Polymeric Materials Science and Engineering (1998), 79, 273-274
CODEN: PMSEGD; ISSN: 0743-0515

PB American Chemical Society

DT Journal

LA English

CC 63-8 (Pharmaceuticals)

AB The hemostatic and air leak capabilities of water-sol. carbodiimide
(WSC)-catalyzed gelatin-poly(L-glutamic acid) (PLGA) hydrogel glue were
superior to those of conventional fibrin glue. This firm adhesion of the
hydrogel glue, along with rapid gelation of the mixt. of gelatin and PLGA
aq. soln., mainly led to higher capabilities of **WSX**-catalyzed
gelatin-PLGA hydrogel glue than fibrin glue.

ST hemostatic adhesive gelatin polyglutamate carbodiimide
 IT Adhesives
 (biol. tissue; hemostatic and air leak sealing effects of rapidly curable glues of gelatin, poly(glutamic acid), and carbodiimide)
 IT Hemostatics
 (hemostatic and air leak sealing effects of rapidly curable glues of gelatin, poly(glutamic acid), and carbodiimide)
 IT Gelatins, biological studies
 Peptides, biological studies
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (hemostatic and air leak sealing effects of rapidly curable glues of gelatin, poly(glutamic acid), and carbodiimide)
 IT Polyamides, biological studies
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (poly(amino acids); hemostatic and air leak sealing effects of rapidly curable glues of gelatin, poly(glutamic acid), and carbodiimide)
 IT Medical goods
 (tissue adhesives; hemostatic and air leak sealing effects of rapidly curable glues of gelatin, poly(glutamic acid), and carbodiimide)
 IT 1892-57-5, 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (hemostatic and air leak sealing effects of rapidly curable glues of gelatin, poly(glutamic acid), and carbodiimide)
 IT 24991-23-9 25513-46-6, Poly(L-glutamic acid)
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (hemostatic and air leak sealing effects of rapidly curable glues of gelatin, poly(glutamic acid), and carbodiimide)

L19 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2002 ACS
 AN 1998:311872 HCAPLUS
 DN 129:77398
 TI Cloning and characterization of a novel class I cytokine receptor
 AU Sprecher, Cindy A.; Grant, Francis J.; Baumgartner, James W.; Presnell, Scott R.; Schrader, Sara K.; Yamagiwa, Tina; Whitmore, Theodore E.; O'hara, Patrick J.; Foster, Donald F.
 CS ZymoGenetics Inc., Seattle, WA, 98102, USA
 SO Biochemical and Biophysical Research Communications (1998), 246(1), 82-90
 CODEN: BBRCA9; ISSN: 0006-291X
 PB Academic Press
 DT Journal
 LA English
 CC 3-3 (Biochemical Genetics)
 Section cross-reference(s): 15
 AB The human gpl30 cDNA sequence was used as a query to search an expressed sequence tag database (dbEST) to identify cDNA sequences with similarity to the cytokine class I receptor family. A novel class I cytokine receptor was identified in a human infant brain cDNA library and was named WSX-1. Full-length cDNA sequences for human and murine WSX-1 were isolated and characterized. The WSX-1 cDNA encodes a 636 amino acid transmembrane protein with an extracellular domain of 482 amino acids and a cytoplasmic domain of 96 amino acids. The structure of the WSX-1 protein most closely resembles that of gpl30. Northern blot anal. indicates high levels of expression in thymus, spleen, lymph node, and peripheral blood leukocytes, suggesting a role for WSX-1 in modulation of the immune

response.

ST human cytokine receptor WSX1 cDNA sequence; map expression cytokine receptor WSX1 sequence; CD4 lymphocyte expression cytokine receptor WSX1

IT Gene, animal
 RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
 (WSX1; expression and map and sequence of; cloning and characterization of novel class I cytokine receptor)

IT Genetic mapping
 Protein sequences
 cDNA sequences
 (cloning and characterization of novel class I cytokine receptor)

IT Protein motifs
 (domain structure diagram contg. IG-like and cytokine-binding and fibronectin type II and cytoplasmic domains; cloning and characterization of novel class I cytokine receptor)

IT Gene
 (expression, tissue-specific gene expression; cloning and characterization of novel class I cytokine receptor)

IT Chromosome
 (human 19, 19p13.11; cloning and characterization of novel class I cytokine receptor)

IT CD4-positive T cell
 Lymph node
 Spleen
 Thymus gland
 (tissue-specific gene expression; cloning and characterization of novel class I cytokine receptor)

IT 200222-32-8, Cytokine receptor Zcytor1 (human clone K7-1-1-P1 gene WSX1 636-amino acid isoform)
 RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
 (amino acid sequence; cloning and characterization of novel class I cytokine receptor)

IT 200222-31-7, GenBank AF053004
 RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
 (nucleotide sequence and tissue-specific expression and map; cloning and characterization of novel class I cytokine receptor)

L19 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2002 ACS

AN 1997:547405 HCAPLUS

DN 127:160574

TI The cytokine **receptor WSX**, **agonist** and antagonist ligands and their uses

IN Bennett, Brian; Carter, Paul J.; Chiang, Nancy Y.; Kim, Kyung Jin; Matthews, William; Rodrigues, Maria L.

PA Genentech, Inc., USA

SO PCT Int. Appl., 219 pp.
 CODEN: PIXXD2

DT Patent

LA English

IC ICM C12N015-12
 ICS C07K014-715; C07K016-46; C07K019-00; C07K016-28; C12N015-62; A61K039-395; C12N005-10; C12N015-85; G01N033-577; G01N033-68

CC 15-5 (Immunochemistry)
 Section cross-reference(s): 1, 13

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI WO 9725425 A1 19970717 WO 1997-US325 19970107
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
CA 2241564 AA 19970717 CA 1997-2241564 19970107
AU 9715747 A1 19970801 AU 1997-15747 19970107
AU 721129 B2 20000622
EP 885299 A1 19981223 EP 1997-901961 19970107
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
JP 2000503204 T2 20000321 JP 1997-525393 19970107
ZA 9700148 A 19980708 ZA 1997-148 19970108
PRAI US 1996-585005 A 19960108
US 1996-667197 A 19960620
WO 1997-US325 W 19970107
AB The cytokine **receptor WSX** that plays a role in hematopoiesis is identified and **antibodies** to it (including **agonist** and neutralizing **antibodies**) are disclosed and uses for them are described. Uses for **WSX** ligands (e.g., anti-**WSX receptor agonist antibodies** or OB protein) in hematopoiesis are also disclosed. The gene for the **receptor** was cloned using probes derived from a human liver expressed sequence tag to screen a Hep3B cDNA library and a full-length clone constructed from several overlapping clones. The **receptor** may play a role in control of cellular proliferation and it is expressed in fetus (lung, liver, kidney) and in adult (liver, placenta, lung, skeletal muscle, kidney, ovary, prostate, small intestine). A no. of variants of the **receptor** were found, of which one (13.2) was a **receptor** for OB protein (leptin). OB protein was found to interact synergistically with interleukin 3, stem cell factor, and GM-CSF in hematopoiesis with a preferential stimulation of myelopoiesis. The identification of **agonist antibodies** is described.
ST **WSX receptor** cytokine leptin; gene **WSX receptor** human mouse; hematopoiesis **WSX receptor** myelopoiesis
IT Immunoglobulins
Immunoglobulins
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(GI, fusion products, with **WSX receptors**, for treatment of **receptor**-dependent disorders; cytokine **receptor WSX, agonist** and antagonist ligands and their uses)
IT Cell proliferation
Erythropoiesis
Hematopoiesis
(**WSX receptor** in; cytokine **receptor WSX, agonist** and antagonist ligands and their uses)
IT Kidney
Liver
Lung
(**WSX receptor** mRNA in fetal and adult; cytokine **receptor WSX, agonist** and antagonist ligands and their uses)
IT Muscle
Ovary
Placenta
Prostate gland

- (**WSX receptor** mRNA in; cytokine **receptor** **WSX**, agonist and antagonist ligands and their uses)
- IT Cytokine **receptors**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(**WSX**; cytokine **receptor** **WSX**, agonist and antagonist ligands and their uses)
- IT **Antibodies**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(agonist or neutralizing, to **WSX receptor** in; cytokine **receptor** **WSX**, agonist and antagonist ligands and their uses)
- IT Chimeric gene
Chimeric gene
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(animal, for **WSX receptor** fusion proteins with Igs; cytokine **receptor** **WSX**, agonist and antagonist ligands and their uses)
- IT Transplant and Transplantation
(bone marrow, stimulation of hematopoiesis through **WSX receptor** in support of; cytokine **receptor** **WSX**, agonist and antagonist ligands and their uses)
- IT Gene, animal
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(cDNA, for **WSX receptor** of human and mouse; cytokine **receptor** **WSX**, agonist and antagonist ligands and their uses)
- IT Gene, animal
Gene, animal
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(chimeric, for **WSX receptor** fusion proteins with Igs; cytokine **receptor** **WSX**, agonist and antagonist ligands and their uses)
- IT Polyoxyalkylenes, biological studies
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(conjugates with **WSX receptors**; cytokine **receptor** **WSX**, agonist and antagonist ligands and their uses)
- IT cDNA sequences
(for **WSX receptor** of human and mouse and for fusion proteins; cytokine **receptor** **WSX**, agonist and antagonist ligands and their uses)
- IT mRNA
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(for **WSX receptor**, tissue distribution in human fetus and adult of; cytokine **receptor** **WSX**, agonist and antagonist ligands and their uses)
- IT Immunoglobulins
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(fusion products, with **WSX receptors**, for treatment of **receptor**-dependent disorders; cytokine **receptor** **WSX**, agonist and antagonist ligands and their uses)
- IT Interleukin 3

Stem cell factor

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(leptin synergism with, in stimulation of myeloproliferation; cytokine **receptor WSX, agonist** and antagonist ligands and their uses)

IT Hematopoiesis

(lymphopoiesis, **WSX receptor** and ligands in stimulation of; cytokine **receptor WSX, agonist** and antagonist ligands and their uses)

IT Hematopoiesis

(myelopoiesis, **WSX receptor** and ligands in stimulation of; cytokine **receptor WSX, agonist** and antagonist ligands and their uses)

IT Protein sequences

(of **WSX receptors** of human and mouse and of fusion proteins; cytokine **receptor WSX, agonist** and antagonist ligands and their uses)

IT Intestine

(small, **WSX receptor** mRNA in; cytokine **receptor WSX, agonist** and antagonist ligands and their uses)

IT Cell

(stem, **WSX receptor** mRNA in; cytokine **receptor WSX, agonist** and antagonist ligands and their uses)

IT Chemotherapy

Radiotherapy

(stimulation of hematopoiesis through **WSX receptor** in support of; cytokine **receptor WSX, agonist** and antagonist ligands and their uses)

IT Bone marrow

(transplant, stimulation of hematopoiesis through **WSX receptor** in support of; cytokine **receptor WSX, agonist** and antagonist ligands and their uses)

IT 193024-85-0P

RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation); USES (Uses)

(amino acid sequence; cytokine **receptor WSX, agonist** and antagonist ligands and their uses)

IT 173015-12-8 193563-66-5 193563-67-6 193563-68-7 193563-71-2

RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(amino acid sequence; cytokine **receptor WSX, agonist** and antagonist ligands and their uses)

IT 169494-85-3, Leptin

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(as ligand for **WSX receptor**; cytokine **receptor WSX, agonist** and antagonist ligands and their uses)

IT 25322-68-3DP, Polyethylene glycol, conjugates with **WSX**

receptors

RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(cytokine **receptor WSX, agonist** and antagonist ligands and their uses)

IT 169494-85-3DP, Leptin, fusion products with Igs

RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (for modulation of **WSX receptor** activity; cytokine **receptor WSX, agonist** and antagonist ligands and their uses)

IT 83869-56-1, GM-CSF

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (leptin synergism with, in stimulation of myeloproliferation; cytokine **receptor WSX, agonist** and antagonist ligands and their uses)

IT 193563-73-4

RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses) (nucleotide sequence; cytokine **receptor WSX, agonist** and antagonist ligands and their uses)

IT 180672-90-6 193563-69-8 193563-70-1 193563-72-3, DNA (mouse **WSX receptor**-specifying)

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study) (nucleotide sequence; cytokine **receptor WSX, agonist** and antagonist ligands and their uses)

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L20 ANSWER 1 OF 4 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 2002:393706 BIOSIS

DN PREV200200393706

TI IL-27, a heterodimeric cytokine composed of EBI3 and p28 protein, induces proliferation of naive CD4+ T cells.

AU Pflanz, Stefan; Timans, Jackie C.; Cheung, Jeanne; Rosales, Rency; Kanzler, Holger; Gilbert, Jonathan; Hibbert, Linda; Churakova, Tatyana; Travis, Marilyn; Vaisberg, Elena; Blumenschein, Wendy M.; Mattson, Jeanine D.; Wagner, Janet L.; To, Wayne; Zurawski, Sandra; McClanahan, Terrill K.; Gorman, Daniel M.; Bazan, J. Fernando; de Waal Malefyt, Rene; Rennick, Donna; Kastelein, Robert A. (1)

CS (1) DNAX Research Institute, 901 California Avenue, Palo Alto, CA, 94304: rob.kastelein@dnax.org USA

SO Immunity, (June, 2002) Vol. 16, No. 6, pp. 779-790.
<http://www.immunity.com/>. print.
ISSN: 1074-7613.

DT Article

LA English

AB An efficient Th1-driven adaptive immune response requires activation of the T cell receptor and secretion of the T cell stimulatory cytokine IL-12 by activated antigen-presenting cells. IL-12 triggers Th1 polarization of naive CD4+ T cells and secretion of IFN-gamma. We describe a new heterodimeric cytokine termed IL-27 that consists of EBI3, an IL-12p40-related protein, and p28, a newly discovered IL-12p35-related polypeptide. IL-27 is an early product of activated antigen-presenting

cells and drives rapid clonal expansion of naive but not memory CD4+ T cells. It also strongly synergizes with IL-12 to trigger IFN-gamma production of naive CD4+ T cells. IL-27 mediates its biologic effects through the orphan cytokine receptor **WSX-1/TCCR**.

CC Cytology and Cytochemistry - Animal *02506

Biochemical Studies - Proteins, Peptides and Amino Acids *10064

Blood, Blood-Forming Organs and Body Fluids - Blood and Lymph Studies *15002

Blood, Blood-Forming Organs and Body Fluids - Blood Cell Studies *15004

Endocrine System - General *17002

Immunology and Immunochemistry - General; Methods *34502

IT Major Concepts

Immune System (Chemical Coordination and Homeostasis)

IT Parts, Structures, & Systems of Organisms

CD4-positive T cell: blood and lymphatics, immune system

IT Chemicals & Biochemicals

EBI3 protein; IFN-gamma; IL-12 [interleukin-12]; IL-27; **WSX-1/TCCR**; p28 protein

IT Miscellaneous Descriptors

adaptive immune response; cell proliferation

L20 ANSWER 2 OF 4 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 2002:186349 BIOSIS

DN PREV200200186349

TI Signaling events and interacting proteins mediated by the cytoplasmic domain of c-mpl.

AU DiPersio, John F. (1); Choi, Luke (1); Holt, Matthew S. (1)

CS (1) Internal Medicine, Washington University School of Medicine, Saint Louis, MO USA

SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 287a.

<http://www.bloodjournal.org/>. print.

Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001

ISSN: 0006-4971.

DT Conference

LA English

AB We have previously mapped critical thrombopoietin (TPO)-induced proliferation regions to Box I and anti-apoptotic effects of TPO to the Box I and Box II regions of the cytoplasmic domain of c-mpl while TPO-induced activation signals such as CD61 and c-fos expression to regions of the c-mpl cytoplasmic domain distal to Box II. We have expressed numerous deletion and site-directed mutants of the cytoplasmic domain of c-mpl in BAF-3 cells. Mutants of c-mpl deleted downstream of Box II were defective in TPO-induced tyrosine phosphorylation of SHC/SHIP, ser/thr phosphorylation and activation of AKT, and increased expression and tyrosine phosphorylation of an unidentified protein, p110, which co-IP using monoclonal antibodies to pBAD ser112. All of these events could be mapped to the penultimate Y626 of c-mpl. In contrast to the upregulation and tyrosine phosphorylation of p110, AKT activation and ser/thr phosphorylation could be inhibited by PI3 kinase inhibitors wortmanin and Ly294002. Kinetics of TPO-induced activation and phosphorylation of p110 and AKT differed with AKT being activated significantly earlier (15 secs) than p110 (5-15 minutes). Murine IL-3, in contrast, induced p110 earlier (15 secs) than AKT (10 minutes). We have utilized yeast 2-hybrid to identify proteins which physically interact with wild type and cytoplasmic deletion mutants of c-mpl fused in frame to hSos (human homolog of yeast cdc25 gene). Various hSos-c-mpl cytoplasmic baits were used to screen a human spleen cDNA library cloned into pMYR vector (CytotrapTM, Stratagene). This system reduced background colony growth and eliminated the problem of bait auto-activation. Two proteins have been identified which physically interact with the wild type hSos-c-mpl cytoplasmic bait. The first protein **WSX-1**, a type I cytokine receptor of unknown function expressed primarily in hematopoietic (lymphoid) cells, was

identified during a screen using hSos-c-mpl bait with regions downstream of Box II deleted. As expected, retransformation assays demonstrated that **WSX-1** binds to both c-mpl cytoplasmic bait which contain the entire cytoplasmic domain of c-mpl as well as with hSos-c-mpl baits in which regions downstream of Box II have been deleted. No interaction between **WSX-1** and hSos-c-mpl baits could be detected when regions downstream of Box I were deleted. The c-mpl interacting domain of **WSX-1** was preliminarily mapped to the transmembrane and cytoplasmic domains of **WSX-1**. The second interacting protein, CXCR4, the chemokine receptor for SDF-1 which is known to functionally synergize with c-mpl, was independently identified in separate screens using two independent hSos-c-mpl baits: one encoding the full length cytoplasmic domain of c-mpl and the other encoding mutant of c-mpl deleted downstream of Box II. Retransformation assays confirmed that the CXCR4 interacting domain of c-mpl resides in the membrane proximal cytoplasmic region of c-mpl including Box I and Box II. Baits lacking Box II did not interact with CXCR4. The c-mpl interacting domain of CXCR4 was preliminarily mapped to the terminal 139 residues (downstream of third transmembrane domain) of CXCR4. Studies to further define interacting domains and critical residues of the distal cytoplasmic region of c-mpl and specific regions of **WSX-1** and CXCR4 which interact with c-mpl and may be involved in TPO-induced signaling in yeast and mammalian 2-hybrid assays are currently underway.

- CC General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
 Cytology and Cytochemistry - Animal *02506
 Cytology and Cytochemistry - Human *02508
 Genetics and Cytogenetics - General *03502
 Genetics and Cytogenetics - Plant *03504
 Genetics and Cytogenetics - Animal *03506
 Genetics and Cytogenetics - Human *03508
 Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
 Biochemical Studies - Proteins, Peptides and Amino Acids *10064
 Biophysics - Membrane Phenomena *10508
 Blood, Blood-Forming Organs and Body Fluids - Blood and Lymph Studies *15002
 Blood, Blood-Forming Organs and Body Fluids - Blood Cell Studies *15004
 Endocrine System - General *17002
 Immunology and Immunochemistry - General; Methods *34502
- BC Fungi - Unspecified 15000
 Hominidae 86215
 Muridae 86375
- IT Major Concepts
 Immune System (Chemical Coordination and Homeostasis); Molecular Genetics (Biochemistry and Molecular Biophysics)
- IT Parts, Structures, & Systems of Organisms
 hematopoietic cell: blood and lymphatics; spleen: blood and lymphatics, immune system
- IT Chemicals & Biochemicals
 AKT: activation, phosphorylation; Box I; Box II; CXCR4: chemokine receptor, interacting domain; IL-3 [interleukin-3]; SDF-1; **WSX-1**: expression, type I cytokine receptor; c-mpl: cytoplasmic domain, mutation; cDNA [complementary DNA]; p110: expression; thrombopoietin; tyrosine: expression, phosphorylation, regulation
- IT Miscellaneous Descriptors
 protein-protein interaction; Meeting Abstract; Meeting Poster
- ORGN Super Taxa
 Fungi: Plantae; Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia; Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
- ORGN Organism Name
 BAF-3 cell line (Muridae): mouse B cells; human (Hominidae); mouse (Muridae); yeast (Fungi)
- ORGN Organism Superterms

Animals; Chordates; Fungi; Humans; Mammals; Microorganisms; Nonhuman
Mammals; Nonhuman Vertebrates; Nonvascular Plants; Plants; Primates;
Rodents; Vertebrates

RN 339184-91-7 (CXCR4)
9014-42-0 (THROMBOPOIETIN)
60-18-4Q (TYROSINE)
556-03-6Q (TYROSINE)

GEN human hSos gene (Hominidae)

L20 ANSWER 3 OF 4 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:527462 BIOSIS
DN PREV200100527462
TI **WSX-1** is required for the initiation of Th1 responses and
resistance to L. major infection.
AU Yoshida, Hiroki; Hamano, Shinjiro; Senaldi, Giorgio; Covey, Todd;
Faggioni, Raffaella; Mu, Sharon; Xia, Min; Wakeham, Andrew C.; Nishina,
Hiroshi; Potter, Julia; Saris, Chris J. M.; Mak, Tak W. (1)
CS (1) The Amgen Institute, University of Toronto, Toronto, Ontario, M5G 2C1:
tmak@oci.utoronto.ca Canada
SO Immunity, (October, 2001) Vol. 15, No. 4, pp. 569-578. print.
ISSN: 1074-7613.
DT Article
LA English
SL English
AB **WSX-1** is a class I cytokine receptor with homology to the IL-12
receptors. The physiological role of **WSX-1**, which is expressed
mainly in T cells, was investigated in gene-targeted **WSX**
-1-deficient mice. IFN-gamma production was reduced in isolated
WSX-1^{-/-} T cells subjected to primary stimulation in vitro to
induce Th1 differentiation but was normal in fully differentiated and
activated **WSX-1**^{-/-} Th1 cells that had received secondary
stimulation. **WSX-1**^{-/-} mice were remarkably susceptible to
Leishmania major infection, showing impaired IFN-gamma production early in
the infection. However, IFN-gamma production during the later phases of
the infection was not impaired in the knockout. **WSX-1**^{-/-} mice
also showed poorly differentiated granulomas with dispersed accumulations
of mononuclear cells when infected with bacillus Calmette-Guerin (BCG).
Thus, **WSX-1** is essential for the initial mounting of Th1
responses but dispensable for their maintenance.

CC Cytology and Cytochemistry - General *02502
Cytology and Cytochemistry - Animal *02506
Immunology and Immunochemistry - General; Methods *34502
Immunology, Parasitological *35000
Parasitology - General *60502
Invertebrata, Comparative and Experimental Morphology, Physiology and
Pathology - Protozoa *64002

BC Flagellata 35200
Muridae 86375

IT Major Concepts
Cell Biology; Immune System (Chemical Coordination and Homeostasis);
Parasitology

IT Parts, Structures, & Systems of Organisms
T cells: blood and lymphatics, immune system; Th1 cells: blood and
lymphatics, immune system

IT Diseases
Leishmania infection: parasitic disease

IT Chemicals & Biochemicals
WSX-1: cytokine receptor

IT Miscellaneous Descriptors
cell differentiation

ORGN Super Taxa
Flagellata: Protozoa, Invertebrata, Animalia; Muridae: Rodentia,
Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
 Leishmania major [L. major] (Flagellata); mouse (Muridae)
 ORGN Organism Superterms
 Animals; Chordates; Invertebrates; Mammals; Microorganisms; Nonhuman
 Mammals; Nonhuman Vertebrates; Protozoans; Rodents; Vertebrates

L20 ANSWER 4 OF 4 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
 AN 1998:266548 BIOSIS
 DN PREV199800266548
 TI Cloning and characterization of a novel class I cytokine receptor.
 AU Sprecher, Cindy A. (1); Grant, Francis J. (1); Baumgartner, James W.;
 Presnell, Scott R. (1); Schrader, Sara K. (1); Yamagiwa, Tina (1);
 Whitmore, Theodore E. (1); O'Hara, Patrick J. (1); Foster, Donald F. (1)
 CS (1) ZymoGenetics Inc., 1201 Eastlake Ave. E., Seattle, WA 98102 USA
 SO Biochemical and Biophysical Research Communications, (May 8, 1998) Vol.
 246, No. 1, pp. 82-90.
 ISSN: 0006-291X.

DT Article
 LA English
 AB The human gp130 cDNA sequence was used as a query to search an expressed
 sequence tag database (dbEST) to identify cDNA sequences with similarity
 to the cytokine class I receptor family. A novel class I cytokine receptor
 was identified in a human infant brain cDNA library and was named
WSX-1. Full-length cDNA sequences for human and murine **WSX**
-1 were isolated and characterized. The **WSX-1** cDNA encodes a 636
 amino acid transmembrane protein with an extracellular domain of 482 amino
 acids and a cytoplasmic domain of 96 amino acids. The structure of the
WSX-1 protein most closely resembles that of gp130. Northern blot
 analysis indicates high levels of expression in thymus, spleen, lymph
 node, and peripheral blood leukocytes, suggesting a role for **WSX**
-1 in modulation of the immune response.

CC Biochemical Studies - Proteins, Peptides and Amino Acids *10064
 Genetics and Cytogenetics - Animal *03506
 Genetics and Cytogenetics - Human *03508
 Comparative Biochemistry, General *10010
 Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062

BC Hominidae 86215
 Muridae 86375

IT Major Concepts
 Molecular Genetics (Biochemistry and Molecular Biophysics)

IT Chemicals & Biochemicals
 WSX-1 cDNA [**WSX-1** complementary DNA]: cloning,
 nucleotide sequence; **WSX-1** gene: chromosomal location;
 WSX-1: amino acid sequence, structure, class I cytokine
 receptor, tissue distribution

IT Miscellaneous Descriptors
 interspecific amino acid sequence comparison

ORGN Super Taxa
 Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia; Muridae:
 Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
 human (Hominidae); murine (Muridae)

ORGN Organism Superterms
 Animals; Chordates; Humans; Mammals; Nonhuman Mammals; Nonhuman
 Vertebrates; Primates; Rodents; Vertebrates

=> d all 8

L23 ANSWER 8 OF 8 MEDLINE
 AN 97455923 MEDLINE
 DN 97455923 PubMed ID: 9310135
 TI Quantitative trait loci associated with promoting effects of sodium

L-ascorbate on two-stage bladder carcinogenesis in rats.
 AU Kamoto T; Mori S; Murai T; Yamada Y; Makino S; Yoshida O; Hiai H
 CS Department of Pathology and Biology of Diseases, Graduate School of
 Medicine, Kyoto University.
 SO JAPANESE JOURNAL OF CANCER RESEARCH, (1997 Jul) 88 (7) 633-8.
 Journal code: 8509412. ISSN: 0910-5050.
 CY Japan
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199710
 ED Entered STN: 19971105
 Last Updated on STN: 19971105
 Entered Medline: 19971023
 AB In the two-stage rat bladder carcinogenesis model using
 N-butyl-N-(4-hydroxybutyl)nitrosamine (BBN) as an initiator and sodium
 L-ascorbate (SA) as a promoter, we found a notable strain difference
 between F344/DuCrj (F344) and WS/Shi (WS) rats in susceptibility to the
 promoting effect of SA. Twenty each of F344, WS and reciprocal F1 hybrid
 rats were given 0.05% BBN in their drinking water for 4 weeks and then a
 basal diet with (BBN-SA group) or without (BBN group) a 5% SA supplement
 for 32 weeks. In F344 and also in reciprocal F1 hybrids, the number of
 tumors per rat was significantly higher in the BBN-SA group than in the
 BBN group ($P < 0.0001$). In contrast, WS rats were not significantly
 affected by either treatment ($P = 0.8$). These findings indicate that F344
 rats are highly susceptible to the promoter effect of SA, but WS rats are
 not. Linkage analysis of 108 WSx (WS x F344) F1 backcrosses
 revealed that this difference was related to a quantitative trait locus
 mapped on rat Chr. 17 (maximum LOD score, 3.86) named Bladder Tumor
 Susceptible-1 and possibly another locus on Chr. 5 (maximum LOD score,
 2.39). This study has provided the first evidence that host genes
 influence the risk of bladder cancer development.
 CT Check Tags: Animal; Male; Support, Non-U.S. Gov't
 *Ascorbic Acid: TO, toxicity
 *Bladder Neoplasms: CI, chemically induced
 *Bladder Neoplasms: GE, genetics
 *Butylhydroxybutyl nitrosamine: TO, toxicity
 *Carcinogens: TO, toxicity
 *Cocarcinogenesis
 Disease Susceptibility
 Drug Synergism
 Rats
 Rats, Inbred F344
 RN 3817-11-6 (Butylhydroxybutyl nitrosamine); 50-81-7 (Ascorbic Acid)
 CN 0 (Carcinogens)

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 Searches in this field may be affected <<<

>>> The BATCH option for structure searches has been

enabled in WPINDEX/WPIDS and WPIX <<<

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L25 ANSWER 1 OF 1 WPIX (C) 2002 THOMSON DERWENT

AN 1997-372864 [34] WPIX

DNN N1997-309574 DNC C1997-120207

TI **WSX** receptor and related antibodies and ligands - used to
develop products for diagnosis and therapy, e.g. for improving
haematopoiesis or for treating tumours.

DC A96 B04 D16 S03

IN BENNETT, B; CARTER, P J; CHIANG, N.Y; KIM, K J; MATTHEWS, W; RODRIGUES, M
L

PA (GETH) GENENTECH INC

CYC 75

PI WO 9725425 A1 19970717 (199734)* EN 219p C12N015-12 <--

RW: AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD
SE SZ UG

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HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX
NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG UZ VN

AU 9715747 A 19970801 (199748) C12N015-12 <--

ZA 9700148 A 19980930 (199844) 166p C07K000-00 <--

EP 885299 A1 19981223 (199904) EN C12N015-12 <--

R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

JP 2000503204 W 20000321 (200025) 285p C12N015-09 <--

AU 721129 B 20000622 (200036) C12N015-12 <--

ADT WO 9725425 A1 WO 1997-US325 19970107; AU 9715747 A AU 1997-15747 19970107,
WO 1997-US325 19970107; ZA 9700148 A ZA 1997-148 19970108; EP 885299 A1 EP
1997-901961 19970107, WO 1997-US325 19970107; JP 2000503204 W JP
1997-525393 19970107, WO 1997-US325 19970107; AU 721129 B AU 1997-15747
19970107

FDT AU 9715747 A Based on WO 9725425; EP 885299 A1 Based on WO 9725425; JP
2000503204 W Based on WO 9725425; AU 721129 B Previous Publ. AU 9715747,
Based on WO 9725425

PRAI US 1996-667197 19960620; US 1996-585005 19960108

REP 5.Jnl.Ref; US 5378808; WO 9101743; WO 9405332; WO 9608510

IC ICM C07K000-00; C12N015-09; C12N015-12

ICS A61K038-00; A61K039-395; A61P001-16; A61P003-00;
A61P003-04; A61P003-06; A61P003-10; A61P007-02; A61P007-04;
A61P007-06; A61P009-00; A61P009-10; A61P009-12; A61P013-12;
A61P017-00; A61P019-02; A61P031-04; A61P035-00; A61P035-02;
A61P037-04; A61P043-00; C07K014-715; C07K016-28;
C07K016-42; C07K016-46; C07K019-00;
C12N005-10; C12N015-02; C12N015-62;
C12N015-85; C12P021-08; G01N033-566; G01N033-577;
G01N033-68

AB WO 9725425 A UPAB: 19970820

An isolated **WSX** receptor is claimed. Also claimed are: (1) an
antibody that specifically binds to a **WSX** receptor; (2) an